that the claims of Group II (Claim 11) be rejoined with those of Group I. Applicant maintains that the Claims of Group I and II are encompassed by the same invention and would be searched in the same art group. Group I is drawn in part to a method for diagnosing a predisposition to psychosis in a progeny comprising determining the presence of anti Cw antibody. Group II is drawn to a method for diagnosing a predisposition to a psychotic disorder comprising determining the presence of anti-Cw antibody. These methods are similar and do not have different functions on effect, as suggested by the Examiner. Both groups provide for methods of diagnosing a predisposition to a psychotic disorder comprising determining the presence of anti-Cw antibody and vary in breadth and scope. Progeny is encompassed by the term "individual" for searching purposes and would not require a separate search, and likewise, the term "psychotic disorder" is encompassed by the term "psychosis", and hence a separate search is not warranted. Thus, the claims perform similar functions and produce similar effects and should not be grouped separately.

Applicant therefore traverses the requirement for restriction, and respectfully requests that it be withdrawn, and that the claims of Groups I and II be rejoined and examined in this application.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-9 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner has stated that in view of the teachings of *In re Wands*, 8 USPQ2d 1400, (1) the experimentation required to diagnose and screen for a predisposition to psychosis would be great as (2) the prior art is silent with respect to screening methods and the detection of maternal anti-Cw antibodies and relating it to psychosis, (3) there are no proper guidance for how to relate the detection of anti-Cw antibodies in a maternal sample to predisposition of psychosis in the progeny in the instant specification, (4) the nature of the invention is a correlation of the presence of the anti-Cw antibody in the maternal biological sample to the predisposition of psychosis in a progeny, (5) the relative skill in the art is high, (6) the state of the prior art has shown to be unpredictable as evidenced by Mouro *et al.*, (7) the claims broadly recite a method

to identify the predisposition of psychosis in progeny by detecting anti-Cw antibody in maternal biological sample without specifically stating how this can be done without undue experimentation. Office Action, page 7. The Examiner maintains that one of skill in the art could not make and use the invention as claimed without undue experimentation. Applicant respectfully disagrees with this conclusion.

For the Examiner's convenience, Applicant will address the issues in the order the presented in the Office Action. First, Applicant's invention relates to a method for diagnosing a predisposition of a progeny to psychosis. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, *e.g., In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (CCPA 1970). Satisfaction of the enablement requirement of §112 is not precluded by the necessity for some experimentation, as long as undue experimentation is not required. *In re Angstadt*, 190 U.S.P.Q. 214, 219 (CCPA1976). In fact, a considerable amount of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Jackson*, 217 U.S.P.Q. 804 (Bd. App. 1982). The experimentation required of the invention for diagnosing a predisposition to psychosis is obtaining a biological sample and determining the presence of an antibody. The experimentation required to accomplish this task is certainly not undue, and can be routinely performed by one of skill in the art.

The Examiner defines the state of the prior art consisting of Bowman *et al.* (*Vox Sang*, 64:226-230 (1993) and Mouro *et al.* (*The Journal of American Society of Hematology*, 6(3):1196-1201 (1995), which are both silent with respect to the detection of anti-Cw antibodies and relating it to psychosis. However, these references do highlight some of the adverse effects determined from the presence of the antibody. No inquiry regarding psychosis of the children are offered. The surviving progeny were not followed for any length of time to establish a link to psychosis. Applicant is claiming a method for determining a predisposition to psychosis. Predisposition means a tendency to a condition that is usually based on the combined effects of genetic and environmental factors. Predisposition confers an increased susceptibility to psychosis. As disclosed in the Application, a link has been established through the case study

presented and other medical evidence indicating a propensity for mental illness from pregnancy complications that may be used in diagnosing a predisposition to schizophrenia. The actual diagnosis of schizophrenia must be made through clinical diagnosis and the invention is providing a tool for use in early diagnosis of a predisposition so that early intervention may be established which can result in a better prognosis. These references do not teach or suggest Applicant's discovery of a link between the presence of the anti-Cw antibody and a predisposition to psychosis.

The Examiner discusses the predictability or lack thereof in the art. The Examiner reiterated that the prior art does not link the presence of anti-Cw antibody to psychosis, but Applicant has and should be entitled to a patent for such discovery. As discussed above, the progeny of the prior art reference have not been followed to determine the presence of Cw antibody indicating a predisposition to psychosis or lack of one. Furthermore, as discussed above, Applicant's claimed invention has provided a link to psychosis, as is detailed in the Specification, in particular as is demonstrated by the case study. It is a tendency to psychosis that is diagnosed through the method, not an absolute indication of psychosis when anti-Cw antibody is detected.

The Examiner questions the guidance available to relate the presence of Cw antibodies to psychotic disorders in the progeny. The claimed invention is a method of diagnosing a predisposition to psychosis. The term "psychosis" encompasses may different mental ailments and other factors must be considered in the clinical diagnosis of psychosis utilizing sources such as *The Diagnostic and Statistical Manual of Mental Disorders* (See Specification page 1, lines 17-21 and page 2, line 23 to page 3, line 2). Applicant has provided significant guidance on determining the presence of anti-Cw antibody and provided the necessary link to psychosis as is demonstrated by the case study.

The Examiner questions the presence of working examples and states that the case study is insufficient. Applicant points out that the mother was tested to be positive for anti-Cw antibody, the father is positive for the antigen, the progeny (who possesses the Cw antigen and was treated for jaundice) and his paternal relatives display psychosis. As indicated in the Specification, page 5, lines 18-29, jaundice results from an attack of antibodies generated by the mother to her progeny's blood antigens. Furthermore, blood antigen incompatibility has been

postulated as a risk factor for schizophrenia (See Hollister *et al.*, *Arch Gen. Psychiatry*, 53:19-24 (1996)). Combined, these factors provide the necessary link, and the case study is sufficient to support the claimed invention. Additionally, there is no requirement for working examples to support the claims, *In re Robbins*, 166 USPQ 552 (CCPA 1970).

The Examiner states that the quantity of experimentation necessary is undue. Applicant respectfully disagrees. The claimed method provides ample description to ascertain the presence of anti-Cw antibody and the presence indicates a predisposition to psychosis. Similar antibody determining assays are conducted routinely at hospitals and other laboratories, and the experimentation is not undue.

The breath of the claims is discussed and the Examiner incorrectly attributes the presence of Cw antigen to a predisposition of a carrier to psychosis. Contrary to the Examiner's conclusion, it is not the mere presence of Cw antigen but the effect of the anti-Cw antibody on the progeny that ultimately predisposes the progeny to psychosis. In the case study, the father is a carrier but does not display psychotic symptoms. As is shown in the study, it is the presence and exposure of anti-Cw antibodies in the progeny who possesses Cw antigen that predisposes the progeny to psychosis. The progeny discussed in the case study displaced signs of psychosis 19 years after his initial exposure to the antibodies.

In view of the remarks provided in response to the Examiner's assessment of the invention, Applicant requests reconsideration and withdrawal of the rejection.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1-10 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states that Claims 1 and 6 are vague, in the recitation of "anti-Cw antibody". The term refers to an antibody to the Cw antigen, as is described in the Specification, page 6 lines 17-20. The term as recited in view of the teachings of the Specification is definite.

Also, the Examiner states that Claim 10 is vague because "it is not clear whether the detector for the anti-Cw antibody is another antibody comprising a label or is it a label reagent used to combine with the anti-Cw antibody for detection purposes". The detector can be both,

another antibody or a label reagent as well as other detection agents that one skilled in the art would have available. A specific agent is not needed to be described but the ability for detection is needed to practice the claimed invention. Applicant's claim as written is clear and definite to one of skill in the art. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §103(a)

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thorpe *et al.* (*Vox Sang* 1997; 73; 174-181) in view of Foster *et al.*, U.S. Patent 4,444,879.

The Examiner states that Thorpe *et al.* teach producing human monoclonal IgG antibodies specific for Cw antigen and that Foster *et al.* teach a kit used for enzyme immunoassays and that it would have been obvious to one of ordinary skill in the art to incorporate into the method of Thorpe *et al.*, a kit comprising all reagents, substrates, controls, etc. Applicant respectfully disagrees.

Applicant's amended claim is drawn to a kit for use in diagnosing a predisposition to psychosis. The cited references do not provide this specific use of a kit or instructions to using the antibody and detector to diagnose a predisposition to psychosis.

Thorpe *et al.* disclose the immunochemical characterization of the RhCw antigen using Human Monoclonal Antibodies. The antibody disclosed by Thorpe *et al.* is an IgG.

Foster *et al.* teach an immunoassay identify immunoglobulins in a sample. Furthermore, Foster *et al.* indicate that " It has also been recognized that IgE materials do not behave in the same way as, for example, IgM or IgG". There is no reasonable expectation of success to combine the IgG immunoglobulin described in Thorpe *et al.* with the method of Foster, as there is no expectation that an IgG would behave properly in Foster's assay given that the assay was designed for Ig, and IgE detection as is demonstrated by the Examples. Additionally, neither reference suggests or motivates one of skill in the art to combine them. Furthermore, the combination of the two references fail to describe or render obvious Applicant's claimed invention: A kit for use in diagnosis of psychosis comprising a sample of anti-Cw antibody, a detector that binds to anti-Cw antibody and instructions for using the antibody and detector to diagnose a predisposition to psychosis. Although the reagents of the kit were known at the time of filing, the use of the kit for diagnosing a predisposition to psychosis was not known prior to

Applicant's invention. Thus, the claimed invention as a whole would not have been obvious to one of ordinary skill in the art at the time the invention was made. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In summary, it is concluded that the art cited by the Examiner does not render obvious Applicant's claimed invention. Accordingly, reconsideration and withdrawal of the rejections are respectfully requested. Should the Examiner believe that prosecution of the application may be expedited by telephone conference with the Applicant's Agent, please call the undersigned at the number given below.

Respectfully submitted,
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Lexington, Massachusetts 02421-4799
Dated: July 25, 2001

MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

10. (Amended) A kit for use in diagnosis of psychosis comprising a sample of anti-Cw antibody, [and] a detector that binds to anti-Cw antibody and instructions for using the antibody and detector to diagnose a predisposition to psychosis.